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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/719,571	09/25/1996	DAVID J. ANDERSON	A-63899-1	9615

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EXAMINER
GRUN, JAMES LESLIE

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/15/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/719,571	ANDERSON
Examiner	**Art Unit**
James L. Grun, Ph.D.	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *6 Aug 2003*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *4-8 and 12-16* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *4-8 and 12-16* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 06 August 2003 has been entered.

Claims 1-3 and 9-11 have been cancelled. Claims 4-8 and 12-16 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 4-8 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant teaches isolation and enrichment of RET+ cells and their culture in cell culture, with or without various additives, in order to characterize the degree of lineage commitment of the cells by analysis of their resultant progeny. However, there is nothing in applicant's written disclosure to teach or suggest how the enrichment procedure could be used to select subpopulations of the RET+ cell population with different particular lineage commitments for use. Indeed applicant admits that the three classes of RET+ progenitor cells were indistinguishable "by expression of any of the antigenic markers examined or by their morphology" (see specification page 25). The cell cultures result in further differentiations of the RET+ cells which result in the loss of the initial RET+ progenitors. Thus there would seem a total inability to select any RET+ progenitor cell subpopulation for any purpose because the results of the culture are required to identify to which subpopulation any given RET+ cell belongs and, as a result of the cell culture, the desired cell subpopulation has already differentiated and been lost for selection and use. In the absence of further written description and guidance from applicant, one would be unable to practice the invention as is now claimed.

Claims 8 and 16, and claims 13-14 as dependent from claim 16, are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Stemple et al (Cell 71: 973-985, 1992) for reasons of record.

Applicant's arguments filed 06 August 2003 have been fully considered but they are again not deemed to be persuasive for the reasons of record that there remains no **factual evidence** of a difference between what is disclosed in the reference and what is instantly claimed. As set forth, the cloned cells of the reference meet the limitations of the substantially pure population as instantly claimed. Applicant's arguments with regard to the different methods of isolation, i.e. "using the method of claim 15" as instantly recited rather than the antibody to LNGFR, cloning, and serial subcloning of the reference, are not dispositive of the issues because the process of making a product does not serve to limit or distinguish the same product made by another method from itself. Applicant's argument again appears drawn to the initially isolated population of the reference which is again not found germane or persuasive with regard to the cloned cells of the reference noted in the rejection. Further, with regard to claim 16 and claims dependent thereupon, applicant admits that at least some of the cells cloned with the method of Stemple et al are also "Nps" (see e.g. specification page 26). The examiner would note again, with regard to claim 8, the disclosure of the reference that cloned cells were obtained which produced only nonneuronal cells such as glial cells (e.g.: page 977, col. 2; Table 2 (G + O); Fig. 7A (G + O)).

As the claims relate to isolation and enrichment of RET+ cells from the neural crest, their cell culture, and the characterization of the lineage commitment of the cultured cells, the following rejection remains applicable:

Claims 4-8 and 12-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lo et al (Perspectives Dev. Neurobiol. 2: 191-201, 1994), Stemple et al (Dev. Biol. 159: 12-23, 1993), Stemple et al (Cell 71: 973-985, 1992), and Martucciello et al for reasons of record.

Applicant's arguments filed 06 August 2003 have been fully considered but they are not deemed to be persuasive. In response to applicant's arguments that RET expression helps to identify particular lineages of neural crest stem cells, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art, i.e. that the isolation of the RET+ cells and further study of their lineage commitment by cell culture should be done, cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Applicant's implication that the speculative development chart in Fig. 6 of Lo et al would teach away from the actual populations isolated is not found persuasive as the various cell populations are recited, in almost all of the instant claims, in the alternative and the reference of Lo et al clearly teaches RET expression in the cells which should be isolated, i.e. autonomic progenitor cells such as the proliferating undifferentiated neural crest precursor cells or those in which the marker persists during stages of lineage commitment including progenitors of neuronal cells and, possibly, glial cells (see e.g. Fig. 6 and page 194). Applicant's arguments are drawn to the results of the lineage analysis, not to the method of isolation and cell culture of RET+ cells as claimed. Again, an invention may be obvious under 35 U.S.C. § 103 even if a great amount of experimentation is

required within the teachings of the prior art so long as that experimentation is within the abilities of one of ordinary skill in the art to carry out, i.e., it is routine.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (703) 308-3980. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (703) 305-3399.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306, or (703) 305-3014, or (703) 308-4242. Official After Final communications, only, can be facsimile transmitted to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. The above inquiries, or requests to supply missing elements from Office communications, can also be directed to the TC 1600 Customer Service Office at phone numbers (703) 308-0197 or (703) 308-0198.

James L. Grun, Ph.D.
September 8, 2003

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641